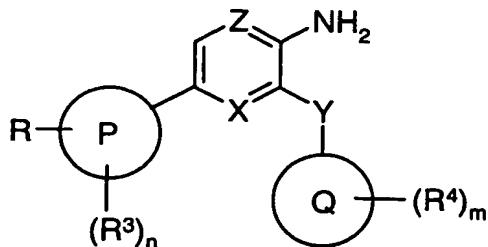


CLAIMS

1. A compound having the formula I



5

wherein:

Z is N;

10 Y is CONR^5 , NR^5CO , SO_2NR^5 , NR^5SO_2 , CH_2NR^5 , NR^5CH_2 , NR^5CONR^5 , $\text{C}_{1-6}\text{alkylene}$, CH_2CO , COCH_2 , $\text{CH}=\text{CH}$, OCH_2 or CH_2O ;

X is CH or N;

15 P is phenyl or a 5 or 6 membered heteroaromatic ring containing one or more heteroatoms independently selected from N, O or S and said phenyl ring or heteroaromatic ring may optionally be fused with a 5 or 6 membered saturated, partially saturated or unsaturated ring containing one or more atoms selected from C, N, O or S;

20 Q is phenyl or a 5 or 6 membered heteroaromatic ring containing one or more nitrogen atoms and said phenyl ring or heteroaromatic ring may optionally be fused with a 5 or 6 membered saturated, partially saturated or unsaturated ring containing one or more atoms selected from C, N, O or S;

25 R is $\text{C}_{1-6}\text{alkylNR}^{10}\text{R}^{11}$ or $\text{C}_{1-6}\text{alkylazetidine}$ which azetidine ring may be optionally substituted by A;

R^3 and R^4 are independently selected from halo, nitro, CHO, C_{0-6} alkylCN, OC_{1-6} alkylCN, C_{0-6} alkylOR⁶, OC_{1-6} alkylOR⁶, fluoromethyl, difluoromethyl, trifluoromethyl, fluoromethoxy, difluoromethoxy, trifluoromethoxy, C_{0-6} alkylNR⁶R⁷, OC_{1-6} alkylNR⁶R⁷, OC_{1-6} alkylOC₁₋₆alkylNR⁶R⁷, NR⁶OR⁷ C_{0-6} alkylCO₂R⁶, OC_{1-6} alkylCO₂R⁶,

5 C_{0-6} alkylCONR⁶R⁷, OC_{1-6} alkylCONR⁶R⁷, OC_{1-6} alkylNR⁶(CO)R⁷, C_{0-6} alkylNR⁶(CO)R⁷, O(CO)NR⁶R⁷, NR⁶(CO)OR⁷, NR⁶(CO)NR⁶R⁷, O(CO)OR⁶, O(CO)R⁶, C_{0-6} alkylCOR⁶, OC_{1-6} alkylCOR⁶, NR⁶(CO)(CO)R⁶, NR⁶(CO)(CO)NR⁶R⁷, SR⁶, C_{0-6} alkyl(SO₂)NR⁶R⁷, OC_{1-6} alkylNR⁶(SO₂)R⁷, OC_{0-6} alkyl(SO₂)NR⁶R⁷, C_{0-6} alkyl(SO)NR⁶R⁷, OC_{1-6} alkyl(SO)NR⁶R⁷, SO₃R⁶, C_{0-6} alkylNR⁶(SO₂)NR⁶R⁷, C_{0-6} alkylNR⁶(SO)R⁷,

10 OC_{1-6} alkylNR⁶(SO)R⁷, OC_{0-6} alkylSO₂R⁶, C_{0-6} alkylSO₂R⁶, C_{0-6} alkylSOR⁶, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{0-6} alkylC₃₋₆cycloalkyl, C_{0-6} alkylaryl and C_{0-6} alkylheteroaryl, wherein any C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{0-6} alkylC₃₋₆cycloalkyl, C_{0-6} alkylaryl and C_{0-6} alkylheteroaryl may be optionally substituted by one or more A;

15 m is 0, 1, 2, 3 or 4;

n is 0, 1, 2, 3 or 4;

R^5 is hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{0-6} alkylC₃₋₆cycloalkyl, C_{0-6} alkylaryl, C_{0-6} alkylheteroaryl, C_{1-6} alkylNR⁶R⁷ or C_{1-6} alkylCONR⁶R⁷;

20 R^6 and R^7 are independently selected from hydrogen, C_{1-6} alkyl, (CO)OR⁸, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{0-6} alkylC₃₋₆cycloalkyl, C_{0-6} alkylaryl, C_{0-6} alkylheteroaryl and C_{1-6} alkylNR⁸R⁹;

25 R^6 and R^7 may together form a substituted 5 or 6 membered heterocyclic ring containing one or more heteroatoms independently selected from N, O or S, which heterocyclic ring may be optionally substituted by A;

30 R^8 and R^9 are independently selected from hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{0-6} alkylC₃₋₆cycloalkyl, C_{0-6} alkylaryl and C_{0-6} alkylheteroaryl;

R^8 and R^9 may together form a 5 or 6 membered heterocyclic ring containing one or more heteroatoms independently selected from N, O or S, which heterocyclic ring may be optionally substituted by A;

5 R^{10} is hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{0-6} alkyl C_{3-6} cycloalkyl, C_{0-6} alkylaryl, C_{0-6} alkylheteroaryl or C_{1-6} alkylNR⁸R⁹;

R^{11} is C_{0-6} alkyl C_{3-6} cycloalkyl;

10 A is halo, nitro, CHO, CN, OR⁶, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{0-6} alkyl C_{3-6} cycloalkyl, fluoromethyl, difluoromethyl, trifluoromethyl, fluoromethoxy, difluoromethoxy, trifluoromethoxy, C_{0-6} alkylNR⁶R⁷, OC C_{1-6} alkylNR⁶R⁷, CO₂R⁸, CONR⁶R⁷, NR⁶(CO)R⁶, O(CO)R⁶, COR⁶, SR⁶, (SO₂)NR⁶R⁷, (SO)NR⁶R⁷, SO₃R⁶, SO₂R⁶ or SOR⁶;

15 as a free base or a pharmaceutically acceptable salt, solvate or solvate of salt thereof.

2. A compound according to claim 1, wherein Z is N; Y is CONR⁵; X is N; P is phenyl; Q is a 6 membered aromatic heterocyclic ring containing one nitrogen atom; R is C_{1-6} alkylNR¹⁰R¹¹; m is 0; n is 0; R⁵ is hydrogen; R¹⁰ is hydrogen or C_{0-6} alkyl C_{3-6} cycloalkyl; C_{0-6} alkylaryl, C_{0-6} alkylheteroaryl or C_{1-6} alkylNR⁸R⁹; and R¹¹ is C_{0-6} alkyl C_{3-6} cycloalkyl.

25 3. A compound according to claim 2, wherein C_{1-6} alkyl in C_{1-6} alkylNR¹⁰R¹¹ represents propyl; R¹⁰ and R¹¹ represents cyclobutyl; and Q represents pyridin.

4. A compound which is:
3-Amino-6-{4-[3-(dicyclobutylamino)propyl]phenyl}-N-pyridin-3-ylpyrazine-2-carboxamide hydrochloride;
as a free base or an alternative pharmaceutically acceptable salt, solvate or solvate of salt thereof

30 5. A compound which is:

3-Amino-6-bromo-*N*-pyridin-3-ylpyrazine-2-carboxamide;

as a free base, a salt, solvate or solvate of a salt thereof.

5 6. A compound which is:

N-[3-(4-Bromophenyl)propyl]-*N,N*-dicyclobutylamine;

as a free base, a salt, solvate or solvate of a salt thereof.

10 7. A pharmaceutical formulation comprising as active ingredient a therapeutically effective amount of a compound according to any one of claims 1 to 4 in association with pharmaceutically acceptable carriers or diluents.

15 8. The pharmaceutical formulation according to claim 7 for use in the prevention and/or treatment of conditions associated with glycogen synthase kinase-3.

9. A compound as defined in any one of claims 1 to 4 for use in therapy.

20 10. Use of a compound according to any one of claims 1 to 4 in the manufacture of a medicament for prevention and/or treatment of conditions associated with glycogen synthase kinase-3.

25 11. Use of a compound according to any one of claims 1 to 4 in the manufacture of a medicament for prevention and/or treatment of dementia, Alzheimer's Disease, Parkinson's Disease, Frontotemporal dementia Parkinson's Type, Parkinson dementia complex of Guam, HIV dementia, diseases with associated neurofibrillar tangle pathologies and dementia pugilistica.

30 12. Use of a compound according to claim 11, wherein the disease is Alzheimer's Disease.

13. Use of a compound according to any one of claims 1 to 4 in the manufacture of a medicament for prevention and/or treatment of amyotrophic lateral sclerosis, corticobasal degeneration, Down syndrome, Huntington's Disease, postencephalitic parkinsonism,

progressive supranuclear palsy, Pick's Disease, Niemann-Pick's Disease, stroke, head trauma and other chronic neurodegenerative diseases, Bipolar Disease, affective disorders, depression, schizophrenia, cognitive disorders, hair loss and contraceptive medication.

- 5 14. Use of a compound according to any one of claims 1 to 4 in the manufacture of a medicament for prevention and/or treatment of predemented states, Mild Cognitive Impairment, Age-Associated Memory Impairment, Age-Related Cognitive Decline, Cognitive Impairement No Dementia, mild cognitive decline, mild neurocognitive decline, Late-Life Forgetfulness, memory impairment and cognitive impairment, vascular dementia, dementia with Lewy bodies, Frontotemporal dementia and androgenetic alopecia and Type I and Type II diabetes, diabetic neuropathy and diabetes related disorders.
- 10 15. A method of prevention and/or treatment of conditions associated with glycogen synthase kinase-3, comprising administrering to a mammal, including man in need of such prevention and/or treatment, a therapeutically effective amount of a compound of formula I as defined in any one of claims 1 to 4.
- 15 16. A method of prevention and/or treatment of dementia, Alzheimer's Disease, Parkinson's Disease, Frontotemporal dementia Parkinson's Type, Parkinson dementia complex of Guam, HIV dementia, diseases with associated neurofibrillar tangle pathologies and dementia pugilistica, comprising administrering to a mammal, including man in need of such prevention and/or treatment, a therapeutically effective amount of a compound of formula I as defined in any one of claims 1 to 4.
- 20 17. The method according to claim 16, wherein the disease is Alzheimer's Disease.
- 25 18. A method of prevention and/or treatment of amyotrophic lateral sclerosis, corticobasal degeneration, Down syndrome, Huntington's Disease, postencephalitic parkinsonism, progressive supranuclear palsy, Pick's Disease, Niemann-Pick's Disease, stroke, head trauma and other chronic neurodegenerative diseases, Bipolar Disease, affective disorders, depression, schizophrenia, cognitive disorders, hair loss and contraceptive medication, comprising administrering to a mammal, including man in need of such prevention and/or

treatment, a therapeutically effective amount of a compound of formula I as defined in any one of claims 1 to 4.

19. A method of prevention and/or treatment of predemented states, Mild Cognitive Impairment, Age-Associated Memory Impairment, Age-Related Cognitive Decline, Cognitive Impairement No Dementia, mild cognitive decline, mild neurocognitive decline, Late-Life Forgetfulness, memory impairment and cognitive impairment, vascular dementia, dementia with Lewy bodies, Frontotemporal dementia and androgenetic alopecia and Type I and Type II diabetes, diabetic neuropathy and diabetes related disorders, comprising administrering to a mammal, including man in need of such prevention and/or treatment, a therapeutically effective amount of a compound of formula I as defined in any one of claims 1 to 4.

20. The use of the intermediates according to claim 5 or 6 for the preparation of a compound of formula I as defined in any one of claims 1 to 4.